[General]

Leukemias: Malignant neoplasms of blood-forming tissues.

Etiology and Pathogenesis

Although viruses cause several forms of leukemia in animals, their role in humans is uncertain; only two viral associations are identified: (1) Epstein-Barr virus, a DNA virus, is associated with Burkitt's lymphoma (see Ch. 139), and (2) human T-cell lymphotropic virus type I, called human T-cell leukemia/lymphoma virus, an RNA retrovirus, is associated with some T-cell leukemias and lymphomas, most commonly identified in Japan and the Caribbean. Exposure to ionizing radiation and certain chemicals (eg, benzene, some antineoplastic drugs) is associated with an increased risk of leukemia. Some genetic defects (eg, Down syndrome, Fanconi's anemia) also predispose to leukemia.

Transformation to malignancy (through two or more steps) occurs in a single cell, with subsequent proliferation and clonal expansion. Usually, transformation occurs at the pluripotent stem cell level, but sometimes it may involve a committed stem cell with capacity for more limited differentiation. The clone tends to be genetically unstable with features of heterogeneity and phenotypic evolution. In general, leukemic cells divide with longer cell cycles and smaller growth fractions than normal bone marrow cells, but they accumulate because of slowed apoptosis (programmed cell death).

Clinical and laboratory features of leukemia are caused by suppression of normal blood cel formation and organ infiltration. Inhibitory factors produced by leukemic cells or replacement of marrow space may suppress normal hematopoiesis, with ensuing anemia, thrombocytopenia, and granulocytopenia. Organ infiltration results in enlargement of the liver, spleen, and lymph nodes, with occasional kidney and gonadal involvement. Meningeal infiltration results in clinical features associated with increasing intracranial pressure (eg, cranial nerve palsies).

Classification

Leukemias were originally termed acute or chronic based on life expectancy but now are classified according to cellular maturity. Acute leukemias consist of predominantly immature cells (usually blast forms); chronic leukemias, more mature cells.

Acute leukemias are divided into lymphoblastic (ALL) and myelogenous (AML) types, which may be further subdivided by morphologic and cytochemical appearance according to the French-American-British (FAB) classification (see Table 138-1) or immunophenotype (see Table 138-2). The specific B-cell and T-cell and myeloid-antigen monoclonal antibodies, together with flow cytometry, are very helpful for classifying ALL versus AML, which is critical for treatment.